

Ophthalmology

Division Photo



Seated: C. West

Outpatient Encounters

Standing: Z. Ahmed, R. Lang, S. Lopper, T. Cook, S. Riazuddin Not Pictured: W. Motley, R. North, M. Bodack, D. Saltarelli, M. Yang, N. Brown, D. Bonsall.

Division Data Summary

Research and Training Details Number of Faculty 13 Number of Joint Appointment Faculty 2 Number of Research Fellows 7 Number of Research Students 3 Number of Support Personnel 16 \$1,312,405 Direct Annual Grant Support Peer Reviewed Publications 23 **Clinical Activities and Training** Number of Clinical Staff 15 Number of Clinical Fellows 1 Number of Other Students 6 Inpatient Encounters 1,548

21,309

Significant Publications

Gerhardt H. Nrarp coordinates endothelial Notch and Wnt signaling to control vessel density in angiogenesis. Dev Cell. 2009; 16: 70-82.

In Phng et al., we have identified a mechanism for integration of the Wnt and Notch pathway during development of retinal blood vessels. This has important implications for the many vascular diseases of the retina.

Li-Kroeger D, Witt LM, Grimes HL, Cook TA, Gebelein B. Hox and senseless antagonism functions as a molecularswitch to regulate EGF secretion in the Drosophila PNS. Dev Cell. 2008; 15: 298-308

These studies identify an important regulatory loop that provides insight into how sensory cells use the Ras-MAPK pathway to induce the formation of additional cell types. Because this pathway is essential for lens formation, retinogenesis, and growth control, this work has important implications for a broad spectrum of eye-related diseases.

Ahmed ZM, Masmoudi S, Kalay E, Belyantseva IA, Mosrati MA, Collin RW, Riazuddin S, Hmani-Aifa M, Venselaar H, Kawar MN, Tlili A, van der Zwaag B, Khan SY, Ayadi L, Riazuddin SA, Morell RJ, Griffith AJ, Charfedine I, Caylan R, Oostrik J, Karaquzel A, Ghorbel A, Friedman TB, Ayadi H, Kremer H. Mutations of LRTOMT, a fusion gene with alternative reading frames, cause nonsyndromic deafness in humans. Nat Genet. 2008; 40: 1335-40

This is the first demonstration of involvement of fusion gene is simple Mendalian disorders. Furthermore, we provided evidence that in the primate lineage LRTOMT evolved from the fusion of two neighboring ancestral genes, which exist as separate genes (Lrrc51 and Tomt) in rodents. The identification of LRTOMT as a new gene involved in hearing loss gives insight for genetic and physiological studies of the inner ear and will help in our understanding of the basic mechanisms underlying normal hearing and in the diagnosis of nonsyndromic deafness.

Qu J, Zhou X, Zhang J, Zhao F, Sun YH, Tong Y, Wei QP, Cai W, Yang L, West CE, Guan MX. Extremely low penetrance of Leber's hereditary optic neuropathy in 8 Han Chinese families carrying the ND4 G11778A mutation. Ophthalmology. 2009; 116: 558-564 e3

Pontoriero GF, Smith AN, Miller LA, Radice GL, West-Mays JA, Lang RA. Dev Biol. 2009; 328: 118-26. In Pontoriero et al., we have shown that E and N cadherins work in concent to regulate morphogensis of the lens. This is an important backdrop for studies of epithelial morphogenesis in vertebrates.

Division Highlights

Zubair Ahmed, PhD

Zubair Ahmed, Ph.D. was one of two new faculty members to join CCHMC and the Division of Pediatric Ophthalmology, during FY2009. Prior to coming to CCHMC, Dr. Ahmed received a Career Development Award (K99) from NIDCD at the National Institutes of Health. Dr. Ahmed studies the genetic causes of Usher Syndrome Type I and, in FY2009; his laboratory identified a new locus for Usher Syndrome Type 1, two novel deafness-causing genes, two new loci for nonsyndromic deafness and twenty new mutations causing hearing loss in human population.

James J. Augsburger, MD

Dr. Augsburger provides ocular oncology servies for the pediatric pediatrics. He is the Chairman of the Department of Ophthalmology at the Unvieristy of Cincinnati Academic Health Care Center.

Marie I. Bodack. OD

Dr. Bodack is focusing on a research project studying exotropia. She is comparing presentations, magnitude of deviation, associated systemic and ocular conditions.

Dean Bonsall, MD

Dr. Bonsall is involved in the Pediatric Eye Disease Investigator Group with clinical trials. These studies are beneficial to patients and the division.

Tiffany A. Cook, PhD

Dr. Cook's laboratory continues their work on deepening our understanding of ocular development, using the fruit fly model, *Drosophila melanogaster*. This year, Dr. Cook served as ad hoc reviewer for two international funding agencies: the German Israeli Foundation for Scientific Research and Development, and the Welcome Trust Research Foundation. Dr. Cook was also a participant of a nationwide National Science Foundation/ASHG-supported Geneticist-Educator Network, which serves as an alliance outreach program. Dr. Cook also served this year as the Director of Recruitment for the University of Cincinnati Molecular and Developmental Biology Graduate Program.

Adam Kaufman, MD

Dr. Kaufman provides specialized care of the cornea and anterior segment of the eye .

Richard A. Lang, PhD

Dr. Lang's laboratory continued making significant scientific contributions during FY2009. His lab has made important advances in our understanding of epithelial morphogenesis mechanisms and has shown that Cdc42-dependent filopodia are critical during the epithelial invagination that results in eye formation. Dr. Lang has also shown that during tissue repair, macrophages produce Wnt pathway ligands to re-capitulate the developmental programs that can re-build a damaged organ. Dr. Lang's research has wide-ranging implications for tissue repair therapies. In FY2009, Dr. Lang and Rashmi Hegde, Ph.D. (Division of Developmental Biology) were awarded a two-year project to investigate how cadherins function in eye development and disease, from the National Eye Institute as part of the America Recovery and Reinvestment Act of 2009.

Sarah Lopper, OD

Dr. Lopper was instrumental in establishing OD Grand Round. These education sessions were very valuable to academic and community optometrist. Dr. Lopper has worked hard to facilitate pathways to ensure regular ophthalmic screenings for children at risk for opthalmic manifestations os systematic diseases.

William Walker Motley, MD

Dr. Motley is managing the Fellowship Program. He is integrating education, research and clinical training into the fellow's education. Dr. Brenda Connors completed the fellowship program and is a practicing pediatric ophthalmologist.

Robert North, DO, MBA, FACS

Dr. North was instrumental in the opening of ophthalmology at the Liberty facility. He provides excellent patient care to patients at the Liberty satellite.

Saima Riazuddin, Ph.D.

Saima Riazuddin, Ph.D. was one of two new faculty members to join CCHMC in FY2009 and she holds a secondary appointment in the Division of Pediatric Ophthalmology and a primary appointment in Division of Otolaryngology. Dr. Riazuddin's research this year focused on characterizing the nonsyndromic deafness gene known as *BSND*. *BSND* has been reported as a disease gene for a severe variant of Barter Syndrome that combines renal salt loss with sensorineural deafness. In November 2008, Dr. Riazuddin was selected as a member of *The Academy of Science for the Developing World* (TWAS).

Dan Saltarelli, OD

Dr. Saltarelli is making a contact lens educational video for parents of patients who require aphakic contact lens. The division anticipates a positive response to this new teaching tool.

Constance West, MD

Dr. West continues to lead the division by teaching several courses outside CCHMC which include: (1) Lancaster; (2) Curso Basico (Puerto Rico); (3) Mexico; and (4) developing academic portfolios for faculty within the division.

Michael Yang, MD

Dr. Yang is working on preliminary ideas for basic science research in ROP and capilllary hemangioma with Dr. Lang and Dr. Cook. The hemangioma research will be complimented by his work in the hemangioma clinic.

Division Collaboration

Collaboration with Developmental Biology

Collaborating Faculty: Jim Wells

Wntless in Pancreas Development with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Aaron Zorn; Rashmi Hegde; Matt Kofron

CRIM1 Function with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Yutaka Yoshida

Wntless in Neurogenesis with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Geraldine Guasch

Sox2 and Wnt in Transitional Zone Formation with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Yi Zheng

GTPase function in morphogenesis with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Noah Shroyer

Wnts in gut regeneration with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Chris Karp

Toll receptor activity in vascular regression with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Xinhua Liu

Wntless function with Richard Lang

Collaboration with Developmental Biology

Collaborating Faculty: Brian Gebelein

Conserved regulatory pathways during Drosophila neurogenesis with Tiffany Cook

Collaboration with Developmental Biology

Collaborating Faculty: Nadean Brown

Photoreceptor differentiation in vertebrates vs. invertebrates with Tiffany Cook

Faculty Members

Constance E. West, MD, Associate Professor; Division Director

James J. Augsburger, MD, FACS, Professor; Chairperson, Department of Ophthalmology

Richard A. Lang, PhD, Professor; Emma & Irving Goldman Scholar; Head, Visual Systems Group

Zubair Ahmed, PhD, Assistant Professor

Marie I. Bodack, OD, FAAO, FCOVD, Instructor Clinical

Dean J. Bonsall, MD, MS, FACS, Associate Professor

Tiffany Cook, PhD, Assistant Professor

Adam H. Kaufman, MD, FACS, Associate Professor

Sarah Lopper, OD, Instructor Clinical

William Walker Motley, MD, MS, Assistant Professor

Robert B. North, DO, MBA, FACS, Assistant Professor

Daniele Saltarelli, OD, Instructor Clinical

Michael B. Yang, MD, Associate Professor

Joint Appointment Faculty Members

Nadean Brown, PhD, Associate Professor Department of Developmental Biology

Saima Riazuddin, PhD, Assistant Professor Department of Otolaryngology

Clinical Staff Members

- Laurie Hahn-Parrott, CO, COT, MBA
- Corey Bowman, COA, LDO, ABOC

- Brandy Dearwater, COA
- o Adrienne Distler, COA
- Jennifer Duncan, COA
- Lisa Fite, COA
- Ashley Jackson, COA
- Debbie Lipps, COA
- Patty Lucas, COA
- Judy Masters, COT
- Nicole McLeod, COA
- Debbie Meister, COA
- Krissy Paddock,
- Kelli Vieson, COT

Trainees

- Elizabeth Agabegi, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Jason Bell, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- April Carpenter-Elrod, PhD, Research Fellow, Hospital for Special Surgery, New York, NY
- Bharesh Chauhan, PhD, Research Associate, Oxford University, Oxford England
- Manpreet Chhabra, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- o lan Conner, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Brenda Connors, MD, Pediatric Ophthalmology Fellow, University of Cincinnati, Cincinnati, OH
- o Jieging Fan, PhD, Graduate Student, Tsinghua University, Beijing, China
- Yueyang Fei, Undergraduate Student, Washington University, St. Louis, MO
- Raja Goli, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- M. Victoria Gomez, Undergraduate Student, Xavier University, Cincinnati, OH
- Michael Gray, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Faiz Khaja, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Rachel Kominsky, Undergraduate Student, Xavier University, Cincinnati, OH
- Lauren Kopicky, Undergraduate Student, Xavier University, Cincinnati, OH
- Elizabeth McDonald, PhD, Graduate Student, Hartwick College, Oneonta, NY
- Elsa Palkovacs, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Timothy Plageman, PhD, Research Fellow, University of Cincinnati, Cincinnati, OH
- Virgilio Ponferrada, PhD, Research Associate, Wright State University, Dayton, OH
- · Sujata Rao, PhD, Research Associate, Cornell University, Ithaca, New York
- Scott Schoenberger, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Eric Speckner, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- · James A. Stefater, MD, PhD, Graduate Student, Centre College, Danville, KY
- Larry Tenkman, MD, Ophthalmology Resident, University of Cincinnati, Cincinnati, OH
- Yoshiaki Ueda, MD, Visiting Research Scientist, National Defense Medical College, Japan
- · Baotong Xie, PhD, Research Fellow, Chinese Academy of Sciences
- Eun-Jin Yeo, PhD, Research Fellow, Seoul National University, Seoul, South Korea

Significant Accomplishments

Pediatric Retina Program at The Abrahamson Pediatric Eye Clinic

The Abrahamson Pediatric Eye Institute and the Division of Pediatric Ophthalmology successfully recruited Dr. Robert Sisk, a vitreoretinal specialist, in FY2009. Dr. Sisk completed both an Internship in Internal Medicine and a Residency in Ophthalmology at the University of Cincinnati. He completed his training with a fellowship in adult and pediatric vitreoretinal surgery at the Bascom Palmer Eye Institute. He will provide care to neonates, infants, and young children at Cincinnati Children's Hospital Medical Center. Dr. Sisk specializes in all medical and surgical diseases of the retina, vitreous. He has special interests in pediatric retinal and surgical diseases, hereditary diseases of the retina, and retinal

electrophysiology. With the addition of Dr. Sisk to the Pediatric Ophthalmology Division, CCHMC can continue to deliver outstanding care to its patient's and families.

Visual Systems Group: Research Accomplishments

The Visual Systems Group of Pediatric Ophthalmology welcomed two new faculty members in FY2009. Zubair Ahmed, Ph.D. and Saima Riazuddin, Ph.D. are both geneticists studying the mechanisms of ocular development and disease in the human population. Their recruitment fulfills the mission of Dr. West and Dr. Lang, and their vision to develop a successful basic science research initiative at CCHMC, focused solely on the development and disease processes of the visual system. The Visual Systems Group, of Pediatric Ophthalmology, is poised to continue their significant contributions to science and translational medicine, well into the next decade.

Division Publications

- Anwar S, Riazuddin S, Ahmed ZM, Tasneem S, Ateeq UI J, Khan SY, Griffith AJ, Friedman TB. <u>SLC26A4 mutation</u> <u>spectrum associated with DFNB4 deafness and Pendred's syndrome in Pakistanis</u>. *J Hum Genet*. 2009; 54: 266-70.
- Yang MB. Extrusion of non-absorbable suture from a supereior oblique tuck without loss of surgical effect.
 Binocul Vis Strabismus Q. 2009; 24: 99-102.
- 3. Le TT, Conley KW, Brown NL. <u>Jagged 1 is necessary for normal mouse lens formation</u>. *Dev Biol.* 2009; 328: 118-26.
- 4. Pontoriero GF, Smith AN, Miller LA, Radice GL, West-Mays JA, Lang RA. <u>Co-operative roles for E-cadherin and N-cadherin during lens vesicle separation and lens epithelial cell survival</u>. *Dev Biol.* 2009; 326: 403-17.
- 5. Willardsen MI, Suli A, Pan Y, Marsh-Armstrong N, Chien CB, El-Hodiri H, Brown NL, Moore KB, Vetter ML. <u>Temporal</u> regulation of Ath5 gene expression during eye development. *Dev Biol.* 2009; 326: 471-81.
- 6. Ahmed ZM, Riazuddin S, Khan SN, Friedman PL, Friedman TB. <u>USH1H, a novel locus for type I Usher syndrome, maps to chromosome 15q22-23</u>. *Clin Genet.* 2009; 75: 86-91.
- Fuhrmann S, Riesenberg AN, Mathiesen AM, Brown EC, Vetter ML, Brown NL. <u>Characterization of a transient TCF/LEF-responsive progenitor population in the embryonic mouse retina</u>. *Invest Ophthalmol Vis Sci.* 2009; 50: 432-40.
- 8. Pediatric Eye Investigator Group, Bonsall DJ, [Collaborator]. Pharmacological plus optical penalization treatment for amblyopia: results of a randomized trial. Arch Ophthalmol. 2009; 127: 22-30.
- Phng LK, Potente M, Leslie JD, Babbage J, Nyqvist D, Lobov I, Ondr JK, Rao S, Lang RA, Thurston G, Gerhardt H. <u>Nrarp coordinates endothelial Notch and Wnt signaling to control vessel density in angiogenesis</u>. Dev Cell. 2009; 16: 70-82.
- 10. Grandy D, Shan J, Zhang X, Rao S, Akunuru S, Li H, Zhang Y, Alpatov I, Zhang XA, Lang RA, Shi DL, Zheng JJ. <u>Discovery and characterization of a small molecule inhibitor of the PDZ domain of dishevelled</u>. *J Biol Chem.* 2009; 284: 16256-63.
- 11. Choi BY, Ahmed ZM, Riazuddin S, Bhinder MA, Shahzad M, Husnain T, Griffith AJ, Friedman TB. <u>Identities and frequencies of mutations of the otoferlin gene (OTOF) causing DFNB9 deafness in Pakistan</u>. *Clin Genet.* 2009; 75: 237-43.
- 12. Qu J, Zhou X, Zhang J, Zhao F, Sun YH, Tong Y, Wei QP, Cai W, Yang L, West CE, Guan MX. MILENTITY MERCHANTE PROPERTY OF THE TOTAL TOTAL
- 13. Riesenberg AN, Le TT, Willardsen MI, Blackburn DC, Vetter ML, Brown NL. <u>Pax6 regulation of Math5 during mouse retinal neurogenesis</u>. *Genesis*. 2009; 47: 175-87.
- Ahmed ZM, Kjellstrom S, Haywood-Watson RJ, Bush RA, Hampton LL, Battey JF, Riazuddin S, Frolenkov G, Sieving PA, Friedman TB. <u>Double homozygous waltzer and Ames waltzer mice provide no evidence of retinal</u> <u>degeneration</u>. *Mol Vis.* 2008; 14: 2227-36.
- 15. Blackburn DC, Conley KW, Plachetzki DC, Kempler K, Battelle BA, Brown NL. <u>Isolation and expression of Pax6</u> and atonal homologues in the American horseshoe crab, <u>Limulus polyphemus</u>. *Dev Dyn.* 2008; 237: 2209-19.
- Li-Kroeger D, Witt LM, Grimes HL, Cook TA, Gebelein B. Hox and senseless antagonism functions as a molecular switch to regulate EGF secretion in the Drosophila PNS. Dev Cell. 2008; 15: 298-308.
- 17. Ahmed ZM, Masmoudi S, Kalay E, Belyantseva IA, Mosrati MA, Collin RW, Riazuddin S, Hmani-Aifa M, Venselaar H, Kawar MN, Tlili A, van der Zwaag B, Khan SY, Ayadi L, Riazuddin SA, Morell RJ, Griffith AJ, Charfedine I, Caylan R, Oostrik J, Karaguzel A, Ghorbel A, Friedman TB, Ayadi H, Kremer H. Mutations of LRTOMT, a fusion gene with alternative reading frames, cause nonsyndromic deafness in humans. Nat Genet. 2008; 40: 1335-40.

- 18. Pediatric Eye Investigator Group, Bonsall DJ, [Collaborator]. <u>A randomized trial of near versus distance activities while patching for amblyopia in children aged 3 to less than 7 years</u>. *Ophthalmology*. 2008; 115: 2071-8.
- 19. Ahmed ZM, Riazuddin S, Aye S, Ali RA, Venselaar H, Anwar S, Belyantseva PP, Qasim M, Friedman TB. <u>Gene structure and mutant alleles of PCDH15: nonsyndromic deafness DFNB23 and type 1 Usher syndrome</u>. *Hum Genet.* 2008; 124: 215-23.
- 20. Chhabra MS, Motley WW, 3rd, Mortensen JE. <u>Eikenella corrodens as a causative agent for neonatal conjunctivitis</u>. *J AAPOS*. 2008; 12: 524-5.
- 21. Swindell EC, Liu C, Shah R, Smith AN, Lang RA, Jamrich M. <u>Eye formation in the absence of retina</u>. *Dev Biol.* 2008; 322: 56-64.
- 22. Ashker L, Weinstein JM, Dias M, Kanev P, Nguyen D, Bonsall DJ. <u>Arachnoid cyst causing third cranial nerve</u> <u>palsy manifesting as isolated internal ophthalmoplegia and iris cholinergic supersensitivity</u>. *J Neuroophthalmol*. 2008; 28: 192-7.
- 23. Rowan S, Conley KW, Le TT, Donner AL, Maas RL, Brown NL. <u>Notch signaling regulates growth and</u> differentiation in the mammalian lens. *Dev Biol.* 2008; 321: 111-22.

Grants, Contracts, and Industry Agreements

University of Cincinnati Research Council

int and Contract Awards	1	Annual Direct / Project Period Direc
ООК, Т.		
Pros/Prox1 and Lens Developme National Institutes of Health	·	
R01 EY 017907	09/15/07 - 07/31/12	\$220,500 / \$1,125,000
ANG, R		
Developing Vision: WNTS In Pro National Institutes of Health	grammed Vessel Regression	
R01 EY 015766	09/23/04 - 08/31/09	\$237,903 / \$1,250,000
Developing Vision: Cadherin Full National Institutes of Health	nction in Lens Morphogenesis	
R01 EY 016241	09/09/05 - 08/31/10	\$237,903 / \$1,250,000
Targeting Survival Factors for O National Institutes of Health (Johns		
R01 EY 012609	04/01/09 - 03/31/12	\$20,400 / \$81,600
Macrophages and Tumor Angiog National Institutes of Health (Alber		
R01 CA 131270	12/01/07 - 11/30/12	\$93,750 / \$468,750
RhoGTPases in Early Eye Develor National Institutes of Health	opment	
R01 EY 017848	04/06/07 - 03/31/12	\$225,000 / \$1,075,000
The Roles of Sox2 in Lens and US-Israel Binational Science Foun	•	
	02/01/09 - 01/31/13	\$15,652 / \$62,608
CRIM1-b-Catenin-Cadherin Inter National Institutes of Health	actions in Eye Development	
R01 EY 019377	06/01/09 - 05/31/11	\$250,000 / \$498,963
EST, C.		
Save Our Sight Ohio Amblyope	Registry	
Ohio Department of Health (Resea		n's Hopsital)
02530011AR0109	07/01/2008 - 6/30/2009	\$6,297 / \$6,297

11/07/08 - 11/06/09

\$5,000 / \$5,000

Total 1,312,405